Prehospital Pharmacology: A Common-Sense Approach

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Definitions:

- **Drugs:** chemical agents used in the diagnosis, treatment, or prevention of disease.
- **Pharmacology:** the study of drugs and their actions on the body.
- **Pharmacokinetics:** the study of the basic processes that determine the duration and intensity of a drug's effect.
- **Pharmacodynamics:** the study of the mechanisms by which specific drug dosages act to produce biochemical or physiological changes in the body.

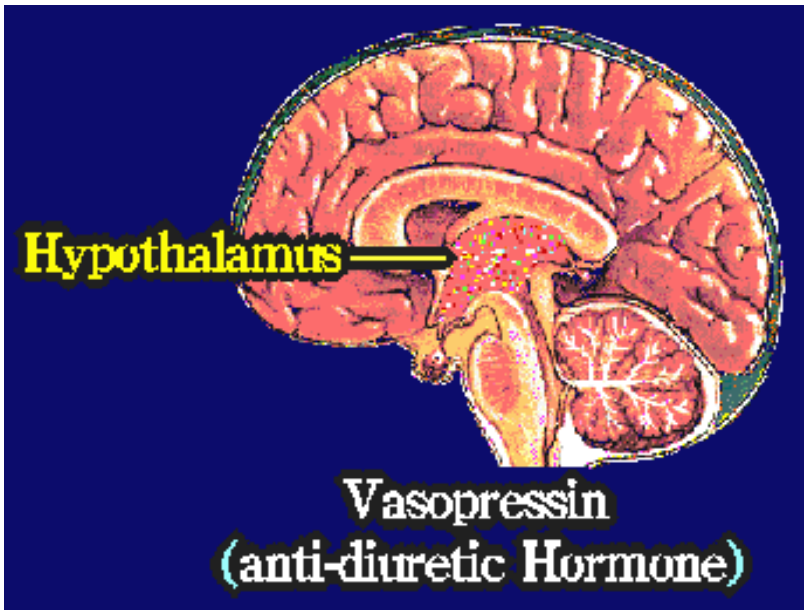
New EMS Drugs

- ***vasopressin***
- ***amiodarone***
- ***etomidate***
- ***fentanyl***
- ***midazolam***
- ***the neuromuscular blockers***

New EMS Drugs

Vasopressin

Vasopressin (Pitressin)



- ***Pharmacological equivalent of* antidiuretic hormone (ADH).**
- ***Secreted from the posterior pituitary.***

Vasopressin (Pitressin)

- ***Controls the amount of water in the body by inhibiting water loss in the kidneys.***
- ***In doses much higher than normally seen in the body it is a potent vasoconstrictor.***

Vasopressin (Pitressin)

- ***Prior to 21st Century, primarily used to slow bleeding in cases of gastrointestinal hemorrhage and for prevention of bedwetting.***
- ***Vasopressin is such a potent vasoconstrictor, when used in the treatment of GI bleeds, intravenous nitroglycerin is often used to prevent tissue and organ ischemia.***
- ***During CPR, animal studies have shown that vasopressin increases blood flow to the brain and heart similar to epinephrine.***

Vasopressin (Pitressin)

- ***However, vasopressin's effects occur through a completely different pharmacological mechanism***
- ***Unlike epinephrine, vasopressin does not appear to exert the same negative effects on the heart in terms of:***
  - ***Ischemia***
  - ***Irritability***
  - ***Ventricular fibrillation***

Vasopressin (Pitressin)

- ***Because most studies on the efficacy of vasopressin in cardiac arrest are animal studies, the AHA gave it a Class IIb recommendation (acceptable, not harmful, supported by only fair evidence).***

Vasopressin (Pitressin)

- ***Current ACLS indications:***
  - ***Ventricular fibrillation***
  - ***Pulseless ventricular tachycardia***
- ***Administer as a single, one-time, 40 unit dose IV early in treatment* in lieu *of epinephrine.***
- ***Half-life of vasopressin is approximately 10-20 minutes (compared to 3-5 minutes for epinephrine.)***

Vasopressin (Pitressin)

- ***If, after the single dose of vasopressin, there is no clinical response in 10-20 minutes, it is acceptable to return to epinephrine every 3-5 minutes.***
- ***Although no human research data supports giving a second dose, there is little potential harm in administering it.***

Vasopressin (Pitressin)

- ***Class:*** *Hormone, vasopressor*
- ***Indications:*** *VF, pulseless VT*
- ***Dose:*** *40 IU IV (single dose only)*
- ***Pharmacokinetics:***
  - ***Absorption:*** *Duration (30-60 m)*
  - ***Distribution:*** *Extracellular fluid*
  - ***Metabolism:*** *Renal, hepatic*
  - ***Elimination:*** *Urine*

Vasopressin (Pitressin)

- ***Contraindications:*** *Few in cardiac arrest*
- ***Adverse/Side Effects:*** *Blanching of skin, abdominal cramps, nausea (almost spontaneously reversible), hypertension, tachycardia, minor dysrhythmias, heart block, peripheral vascular collapse, coronary insufficiency, MI*
- ***Interactions:*** *None with common ACLS drugs*

Vasopressin (Pitressin)

- ***Prehospital Considerations:***
  - *Conclusive evidence supporting the use of vasopressin in cardiac arrest is lacking (Class IIb)*
  - *May be useful in septic shock in conjunction with other inotropic agents.*

New EMS Drugs

Amiodarone

Amiodarone (Cordarone)

- ***Potent antidysrhythmic that blocks both α and β adrenergic properties.***
- ***Pharmacological mechanisms are complicated affecting the sodium, potassium, and calcium ion channels thus prolonging the duration of the action potential and the refractory period.***
- ***Acts directly on cardiac tissues.***
- ***Unrelated to any other antidysrhythmic agent.***

Amiodarone (Cordarone)

- ***In higher doses, it decreases peripheral vascular resistance and increases coronary artery blood flow.***
- ***Blocks the effects of sympathetic stimulation.***
- ***Indicated for ventricular fibrillation and pulseless ventricular tachycardia refractory to multiple shocks.***

Amiodarone (Cordarone)

- ***Initial dose of amiodarone in shock-resistant VF and pulseless VT is 300 mg IVP.***
- ***If dysrhythmia persists, a second 150 mg dose can be administered.***
- ***Maximum dose of amiodarone is 2.2 grams over 24 hours.***

Amiodarone (Cordarone)

- ***Presently, AHA has given amiodarone a Class IIb recommendation (acceptable, not harmful, supported by only fair evidence).***

Amiodarone (Cordarone)

- ***Studies on effectiveness of amiodarone have been controversial:***
  - ***Limited number of human cardiac arrest studies available***
  - ***Recent study showed increased survival to hospital admission in patients who received amiodarone instead of lidocaine. (New England Journal of Medicine* 2002 Mar 21;346(12):884-90)**

Amiodarone (Cordarone)

- ***Cost can be a major consideration in prehospital use of amiodarone.***
- ***Single dose of amiodarone costs 10-20 times that of a single dose of lidocaine.***

Amiodarone (Cordarone)

- ***Class:*** *Antidysrhythmic*
- ***Indications:*** *VF, VT, supraventricular dysrhythmias.*
- ***Dose:***
  - ***VF/VT:*** *300 mg IV; may repeat at 150 mg*
  - ***Refractory VT:*** *150 mg IVP*
  - ***Refractory SVTs:*** *150 mg IVP*
- ***Pharmacokinetics:***
  - ***Absorption:*** *Drops to 10% of peak value in 30-45 mins*
  - ***Distribution:*** *Widespread*
  - ***Metabolism:*** *Hepatic (half-life 40-55 days)*
  - ***Elimination:*** *Bile*

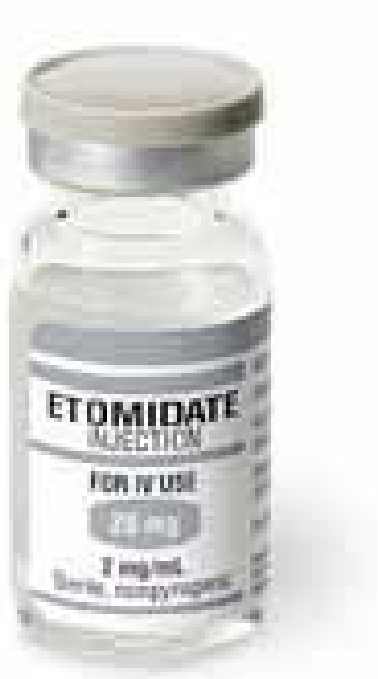
Amiodarone (Cordarone)

- ***Contraindications:*** *Cardiogenic shock, severe sinus bradycardia, or advanced AV blocks.*
- ***Adverse/Side Effects:*** *Dizziness, weakness, headache, bradycardia, hypotension, cardiogenic shock, CHF, dysrhythmias, AV block, nausea, vomiting, constipation*
- ***Interactions:*** *Can significantly increase digoxin levels. Increases effects of lidocaine and procainamide.*

Amiodarone (Cordarone)

- ***Prehospital Considerations:***
  - *Carefully monitor the BP during IV infusion. Slow the infusion if hypotension ensues.*
  - *Sustained monitoring is required because of the long half-life*

New EMS Drugs



Etomidate

Etomidate (Amidate)

- ***Increased recent usage as hypnotic for RSI.***
- ***Ultra-short-acting, nonbarbiturate, nonbenzodiazepine hypnotic.***
- ***NO analgesic properties whatsoever.***
- ***Produces rapid state of sedation suitable for RSI.***

Etomidate (Amidate)

- ***Advantageous over many other hypnotics as it does not cause histamine release.***
- ***Respiratory and cardiovascular effects are minimal.***
- ***Limited studies have a slight increase in RSI success rate in prehospital care where etomidate is used instead of midazolam.***

Etomidate (Amidate)

- ***Induction dose is 0.1-0.3 mg/kg IV over 15-30 seconds.***
- ***Onset of action begins within 10-20 seconds, peaks within 1 minute, and last for 3-5 minutes.***
- ***Should not be used in children less than 10 years of age.***
- ***Pediatric dose same as the adult dose.***
- ***Does not appear to have abuse potential and is not scheduled.***

Etomidate (Amidate)

- ***Class:*** *Hypnotic*
- ***Indications:*** *Induction agent for RSI.*
- ***Dose:*** *0.1-0.3 mg/kg IV*
- ***Pharmacokinetics:***
  - ***Absorption:*** *Onset 10-20 seconds; peak effects at 1 minute; duration is 3-5 minutes*
  - ***Distribution:*** *Widespread*
  - ***Metabolism:*** *Hepatic (half-life 30-74 minutes)*
  - ***Elimination:*** *Urine*

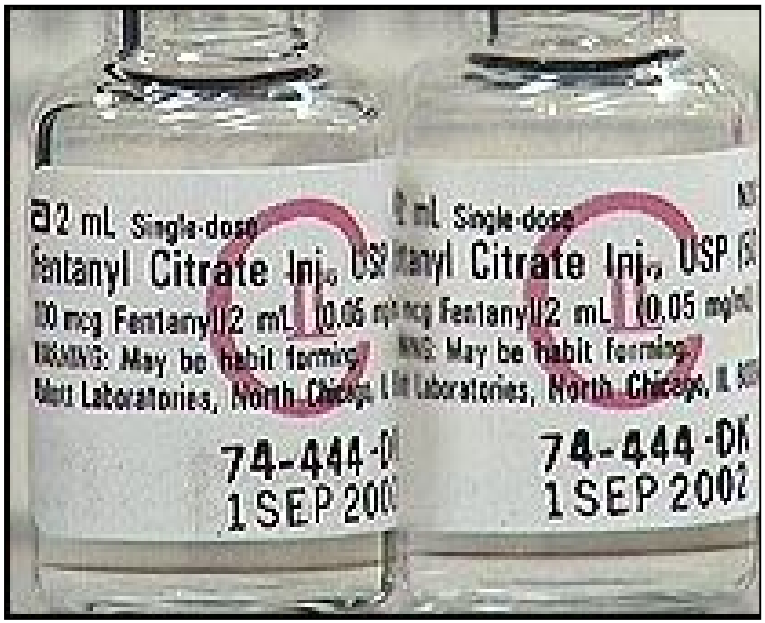
Etomidate (Amidate)

- ***Contraindications:*** *Patients with known hypersensitivity to the drug. Use with caution with marked hypotension, severe asthma, and patients with marked CV disease.*
- ***Adverse/Side Effects:*** *Myoclonic skeletal muscle movements, tonic movements, apnea, hyperventilation or hypoventilation, laryngospasm, hypotension or hypertension, tachycardia, bradycardia, nausea, vomiting.,*
- ***Interactions:*** *None in emergency setting.*

Etomidate (Amidate)

- ***Prehospital Considerations:***
  - *Verapamil may prolong respiratory depression/apnea*
  - *Etomidate does NOT have analgesic properties*
  - *Nausea is common*
  - *Myoclonic jerks are common*
  - *Flumazenil DOES NOT reverse effects*
  - *Should not be used in children less than 10 years*

New EMS Drugs



Fentanyl

Fentanyl (Sublimaze)

- ***Potent synthetic narcotic with properties similar to those of meperidine and morphine***
- ***Chemically unrelated to morphine, but 50-100 times more potent***
- ***Duration of action is considerably shorter than both morphine and meperidine.***

Fentanyl (Sublimaze)

- ***Used in EMS for analgesia and sedation.***
- ***Less negative effects on BP and respirations compared to morphine.***
- ***Less nausea and vomiting compared to morphine and meperidine.***

Fentanyl (Sublimaze)

- ***In EMS, used for moderate to severe pain, and as an adjunct for facilitated intubation.***
- ***Typical starting dose is 25-100 µgs (0.025-0.1 mg) administered slow IVP over 2-3 minutes.***
- ***Pediatric dose is 2.0 µgs/kg slow IVP.***

Fentanyl (Sublimaze)

- ***Fentanyl has a very high potential for abuse and habituation.***
- ***Schedule II Controlled Substance***

Fentanyl (Sublimaze)

- ***Class:*** *Narcotic analgesic*
- ***Indications:*** *Adjunct agent for RSI and for moderate to severe pain.*
- ***Dose:*** *25-100 µg slow IVP*
- ***Pharmacokinetics:***
  - ***Absorption:*** *Onset immediate; peak effect at 3-5 mins, duration is 30-60 minutes*
  - ***Distribution:*** *Widespread*
  - ***Metabolism:*** *Hepatic*
  - ***Elimination:*** *Urine*

Fentanyl (Sublimaze)

- ***Contraindications:*** *Patients who have received MAO inhibitors within 14 days, myasthenia gravis. Use with caution in head injuries and increased ICP, elderly, debilitated, and COPD.*
- ***Adverse/Side Effects:*** *Sedation, euphoria, dizziness, diaphoresis, delirium, hypotension, bradycardia, nausea, vomiting, laryngospasm, respiratory depression.*
- ***Interactions:*** *Alcohol and other CNS depressants; MAO inhibitors.*

Fentanyl (Sublimaze)

- ***Prehospital Considerations:***
  - *Parenteral dose may be given diluted or undiluted*
  - *Administer over 1-2 minutes*
  - *Protect from light*
  - *Monitor vital signs*
  - *Respiratory depression may last longer than analgesic effect.*
  - *May be reversed by naloxone (Narcan)*

New EMS Drugs

Midazolam

Midazolam (Versed)

- ***Short-acting sedative hypnotic***
- ***Benzodiazepine and thus shares many features with diazepam (Valium)***
- ***Water-soluble***
- ***CNS depressant and causes significant amnesia following administration***

Midazolam (Versed)

- ***Has some muscle relaxant and anticonvulsant properties (although these are less pronounced than with diazepam).***
- ***Thus serves to calm and sedate patients, relax skeletal muscles, and, in high doses, causes sleep.***
- ***Midazolam DOES NOT have analgesic properties.***

Midazolam (Versed)

- ***In EMS, it is used to induce sedation and amnesia prior to painful procedures.***
- ***Also used as an induction agent for RSI.***
- ***Typical adult dose is 1.0-2.5 mg slow IVP.***
- ***Pediatric dose is 0.05-0.20 mg/kg slow IVP***

Midazolam (Versed)

- ***All physiological monitors must be in place prior to administering midazolam.***
- ***Flumazinil is an effective antagonist.***

Midazolam (Versed)

- ***Class:*** *Sedative/hypnotic*
- ***Indications:*** *Induction agent for RSI and for sedation prior to painful procedures.*
- ***Dose:*** *1.0-2.5 mg slow IVP*
- ***Pharmacokinetics:***
  - ***Absorption:*** *Onset in 3-5 minutes; peak effect at 20-60 mins, duration is less than 2 hours*
  - ***Distribution:*** *Widespread; crosses BBB and placenta*
  - ***Metabolism:*** *Hepatic*
  - ***Elimination:*** *Urine*

Midazolam (Versed)

- ***Contraindications:*** *Patients with known hypersensitivities to the drug. Use with caution in COPD, CRF, CHF, and the elderly.*
- ***Adverse/Side Effects:*** *Retrograde amnesia, headache, euphoria, drowsiness, excessive sedation, confusion, hypotension, nausea, vomiting, coughing, laryngospasm, respiratory arrest.*
- ***Interactions:*** *Alcohol and other CNS depressants.*

Midazolam (Versed)

- ***Prehospital Considerations:***
  - *When given IM, give deep into the gluteus, not the deltoid*
  - *IV midazolam can be diluted to give a concentration of 0.25 mg/mL*
  - *Effects can be reversed with midazolam, if necessary.*
  - *All resuscitative equipment must be available prior to administering midazolam*

New EMS Drugs

Neuromuscular Blockers

Neuromuscular Blockers

- ***Establishment and protection of the airway has the highest priority in emergency care.***
- ***Difficulty encountered with:***
  - ***CHI (GCS ≤ 8)***
  - ***Status epilepticus***
  - ***Drug overdose***
- ***Neuromuscular blockers cause total muscle relaxation this facilitating endotracheal intubation.***

Neuromuscular Blockers

- ***All skeletal muscles, including the muscles of respiration, respond to these drugs.***
- ***Following administration, the patient will become apneic and require mechanical ventilation.***
- ***Have NO EFFCT on the patient's level of consciousness.***

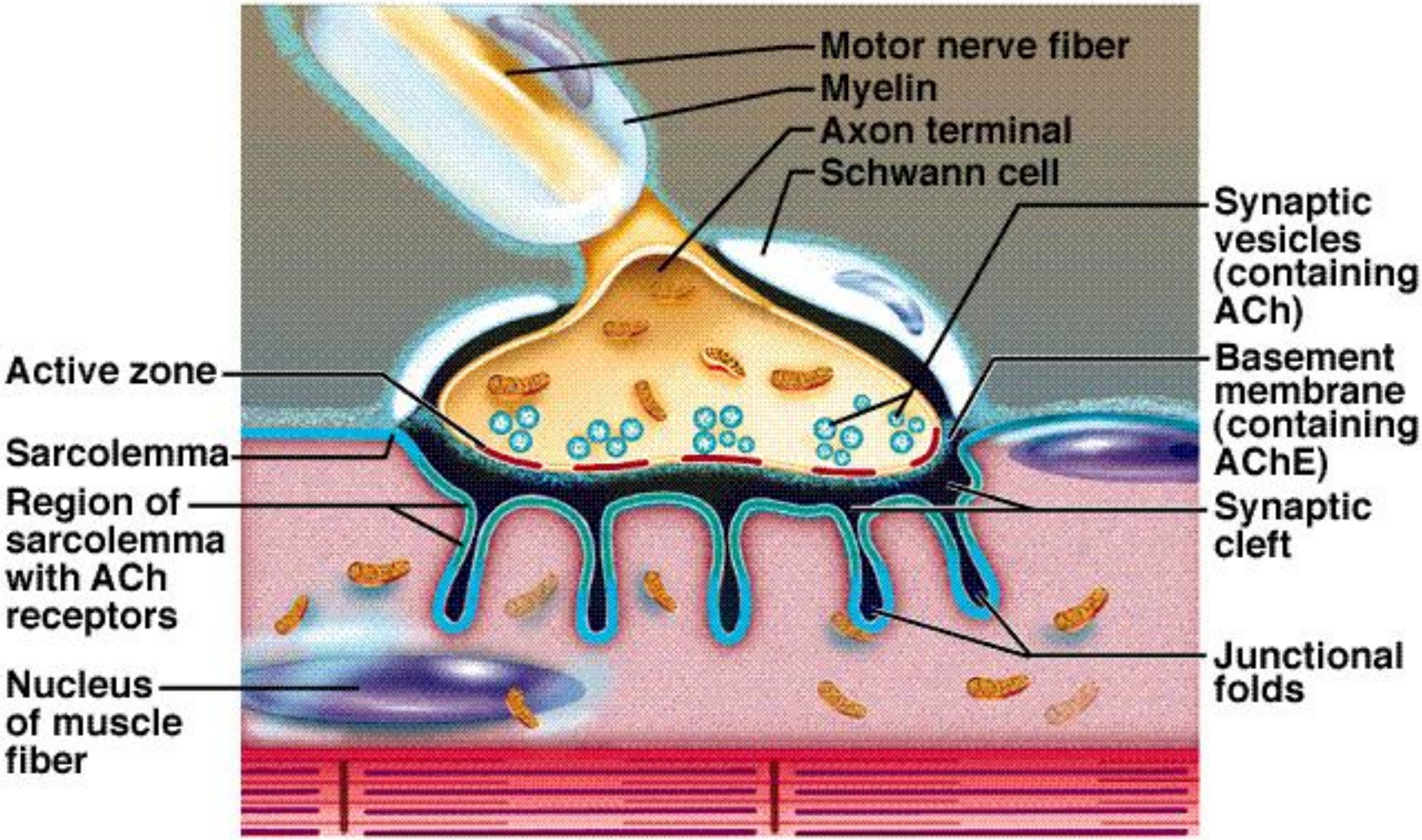
Neuromuscular Blockers

- ***Classifications:***
  - ***Depolarizing:***
    - ***Succinylcholine***
  - ***Non-depolarizing:***
    - ***Pancuronium***
    - ***Vecuronium***
    - ***Atracurium***
    - ***Rocuronium***
    - ***Mivacurium***

Depolarizing Agents

- ***Succinylcholine has a biphasic effect:***
  - ***Phase 1: Acts like acetylcholine and depolarizes the synaptic membranes of the muscle.***
    - ***Not deactivated by acetylcholinestersae***
    - ***Causes muscle fasiculations, followed by muscle paralysis and flaccidity.***
  - ***Phase 2: Not seen, except in high concentrations***
    - ***Causes receptor site blockade and continued paralysis***

Neuromuscular Junction



Non-Depolarizing Agents

- ***Also called competitive or stabilizing agents.***
- ***Similar to curare alkaloids.***
- ***Compete with acetylcholine at the NMJ.***
- ***Blocks the effects of acetylcholine thus causing muscle paralysis and flaccidity.***
- ***Can be counteracted clinically by anticholinesterase drugs (neostigmine, pyridostigmine).***

Non-Depolarizing Agents

- ***Initial muscle weakness quickly changes to flaccid paralysis.***
- ***First muscles affected are those innervated by the cranial nerves (eyes, face, and neck).***
- ***Followed by:***
  - ***Limb***
  - ***Abdomen***
  - ***Trunk***
  - ***Intercostals and diaphragm***
- ***Recovery usually occurs in reverse order***

Non-Depolarizing Agents

- ***These drugs do not cross the BBB and thus DO NOT affect mental status or pain.***
- ***Nondepolarizing blockers are used for intermediate and prolonged muscle relaxation.***
  - ***Facilitated intubation***
  - ***Muscle relaxation for surgery***
  - ***Continued mechanical ventilation***
  - ***Prevent additional injury (penetrating globe injuries)***

Succinylcholine (Anectine)

- ***Two-linked acetylcholine molecules***
- ***Depolarizing blocker***
- ***Acts in 30-60 seconds***
- ***Lasts 4-5 minutes***
- ***Causes initial fasiculations progressing to total paralysis.***

Pancuronium (Pavulon)

- ***Non-depolarizing blocker.***
- ***Long-acting***
- ***Acts in 2-3 minutes***
- ***Lasts approximately 65 minutes.***

Vecuronium (Norcuron)

- ***Non-depolarizing blocker.***
- ***Short-acting***
- ***Acts in 2.5-3.0 minutes***
- ***Lasts 25-30 minutes.***

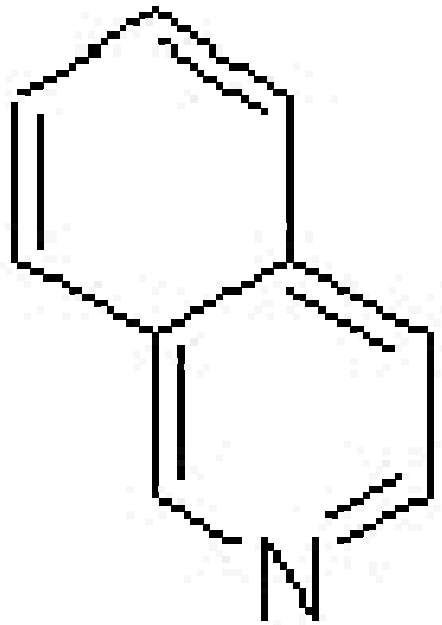
Rocuronium (Zemuron)

- ***Non-depolarizing blocker.***
- ***Rapid- to intermediate-acting (dose-dependent)***
- ***Acts in 2 minutes***
- ***Lasts for up to 30 minutes.***

Atracurium (Tracrium)

- ***Non-depolarizing blocker.***
- ***Intermediate- to long-acting.***
- ***Acts in 3-5 minutes.***
- ***Lasts approximately 60 minutes.***

Mivacurium (Mivacron)



- ***Non-depolarizing blocker.***
- ***Short-acting***
- ***Acts in 3 minutes.***
- ***Lasts for 15-20 minutes.***

Generic	*Trade*	*Class*	*Adult*	*Pedi*	*Onset*	*Duration*
succinylcholine	Anectine	Depolarizing	1.0-1.5 mg/kg	1.0-2.0 mg/kg	0.5-1.0	2-3
vecuronium	Norcuron	Nondepolarizing	0.04-0.1 mg/kg	1 y: adult dose	2.5-3.0	25-30
atracurium	Tracrium	Nondepolarizing	0.4-0.5 mg/kg	1 mo-2 y: 0.3-0.4 mg/kg > 2 y: adult dose	3-5	60
rocuronium	Zemuron	Nondepolarizing	0.6 mg/kg	0.6 mg/kg	2	30
mivacurium	Mivacron	Nondepolarizing	0.15 mg/kg	2-12 y: 0.2 mg/kg	3	15-20
pancuronium	Pavulon	Nondepolarizing	0.04-0.1 mg/kg	0.04-0.1 mg/kg	2	65

Controversies in Prehospital Pharmacology

- ***N.A.V.E.L. administration***
- ***Thiamine and the "Coma Cocktail"***
- ***tPA for CVA***

N.A.V.E.L.

- ***Despite lack of scientific evidence, some still teach the mnemonic:***

N = naloxone

A = atropine

V = Valium

E = epinephrine

L = lidocaine

N.A.V.E.L.

- ***There is no evidence that diazepam can be administered endotracheally.***
- ***Reasons include:***
  - ***Low pH***
  - ***Caustic preservatives***
  - ***Inability to dilute in the field***

N.A.V.E.L.

- ***If mnemonics are used, then consider:***
  - ***LEAN***
  - ***LANE***

“Coma Cocktails”

- ***Some have advocated administering a “coma cocktail” to unconscious patients of unknown etiology.***

NO MORE Coma Cocktails

Using science to dispel myths & improve patient care

By Bryan E. Bledsoe, DO, FACEP, EMT-P

MANY EMS PRACTICES HAVE EVOLVED with a lack of scientific evidence to support them. The MAST/PASG device is a good example of this. When formally investigated, the purported physiological effects of the device couldn't be demonstrated. Now, with scientific knowledge, MAST/PASG serves a much more limited role in modern EMS.

It's curious that practices often adopted by the EMS community come virtually out of nowhere. *Example:* teaching the mnemonic NAVEL (referring to naloxone, atropine, Valium, epinephrine and lidocaine) to remember the five drugs that supposedly could be administered via a properly placed endotracheal tube.

There's absolutely no scientific evidence to support the recommendation that diazepam (Valium) can be administered endotracheally. First, it's not water-soluble; it can be diluted only in alcohol. Medications administered endotracheally must be diluted in a solvent to deliver an adequate volume of the drug to the respiratory tree. Because most ambulances don't carry ethyl alcohol as a solvent, it's impossible to dilute diazepam.

Second, the low pH of diazepam and the presence of preservatives and solvents could potentially damage sensitive pulmonary tissues. When studied in animal models, endotracheal diazepam inflamed pulmonary tissues and adversely impacted respiratory gas exchange.

Similar misconceptions have resulted in some EMS systems touting the advantage of a "coma cocktail" in treating unconscious people.

The coma cocktail

The coma cocktail consists of 50% dextrose solution, the narcotic antagonist naloxone (Narcan) and thiamine (vitamin B1). In some regions, the benzodiazepine antagonist flumazenil (Romazicon) is also administered. Some systems administer this series of medications in rapid succession in an attempt to determine possible causes for unconsciousness.

I wonder what paralysis of intellect gave birth to this idea. This is equivalent to going duck hunting and shooting three or four shotgun rounds at a flock of birds hoping you'll hit the single mallard flying in the middle. EMS is

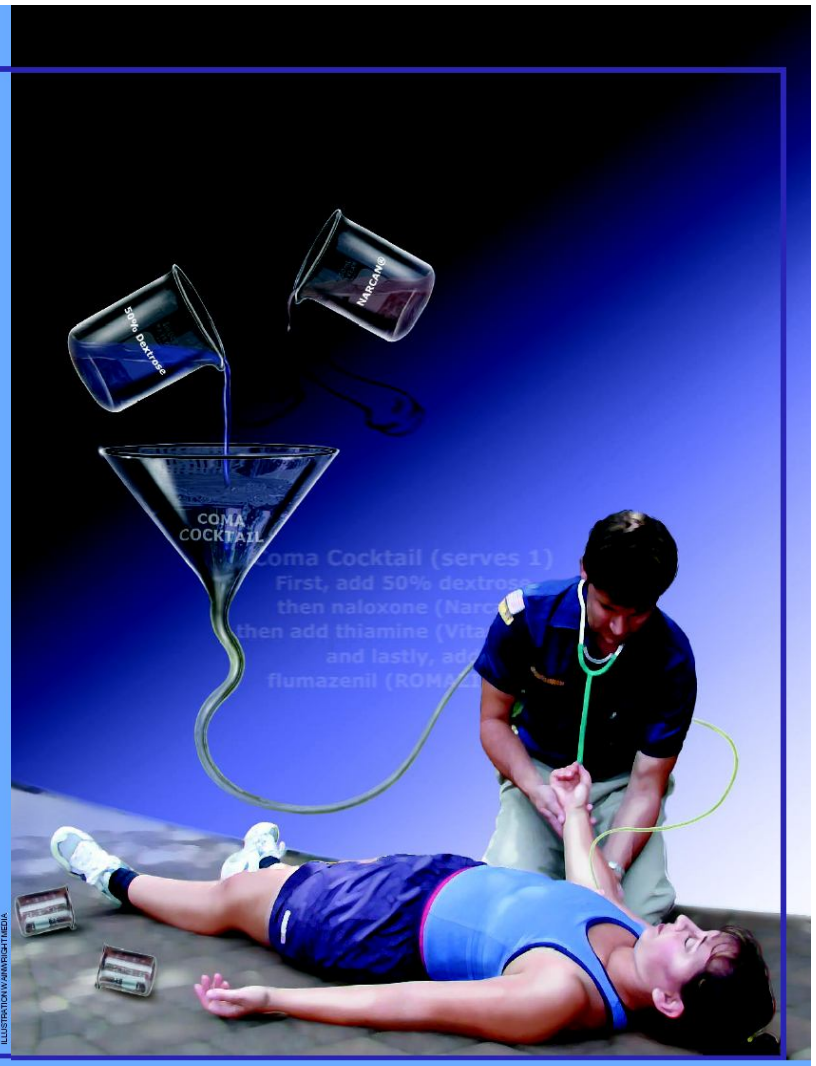


ILLUSTRATION ©JANRIGHTMEDIA

"Coma Cocktails"

- ***Some have advocated giving:***

1. ***Thiamine***
2. ***50% dextrose***
3. ***Naloxone***
4. ***Flumazenil***

to all unconscious patients of unknown etiology.

“Coma Cocktails”

Imagine the paralysis of intellect that gave birth to this idea.

"Coma Cocktail"

- ***Any EMS person with even a small amount of field experience should be able to narrow down the potential causes of unconsciousness without administering "diagnostic medication."***

50% Dextrose

- ***Indicated for hypoglycemia.***
- ***Hypoglycemia results from:***
  - ***Excess insulin dose***
  - ***Inadequate calories following normal insulin dose***

50% Dextrose

- ***Incidence of bonafide hypoglycemia in adults who do not have diabetes mellitus is exceedingly rare.***
- ***Causes include:***
  - ***Very extreme stress states***
  - ***Insulinomas***
  - ***Intoxication with certain drugs (beta blockers, ethanol, and sulfonylureas)***

50% Dextrose

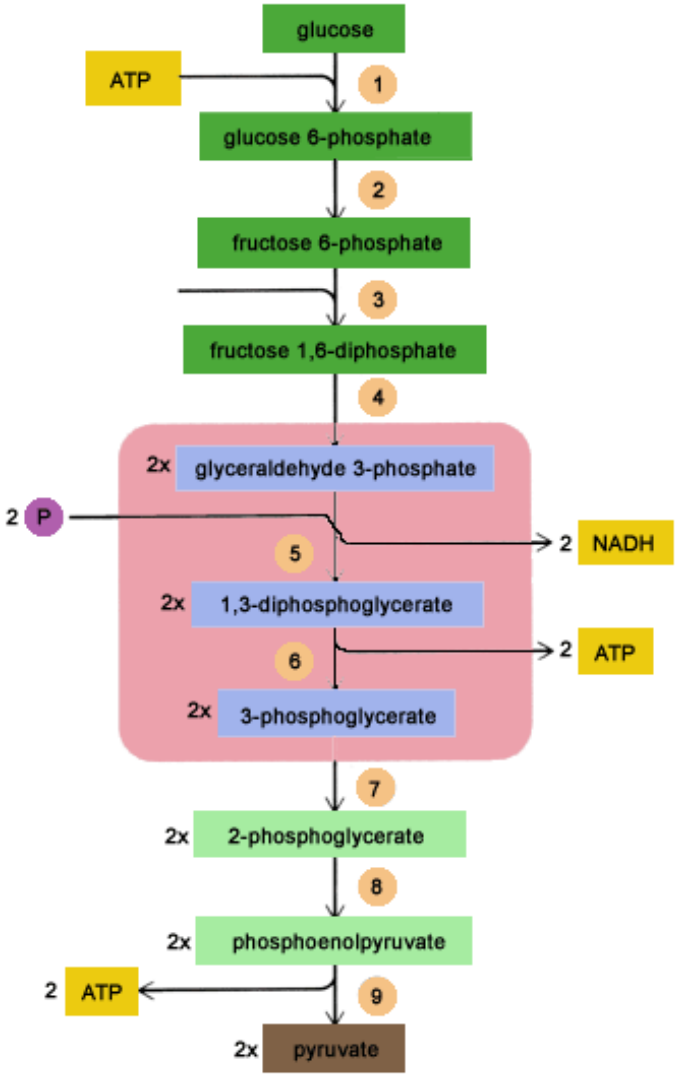
- ***In a study of 926 adult trauma patients with a GCS < 15, only 4 cases of hypoglycemia were found and only one of these was in a non-diabetic.***

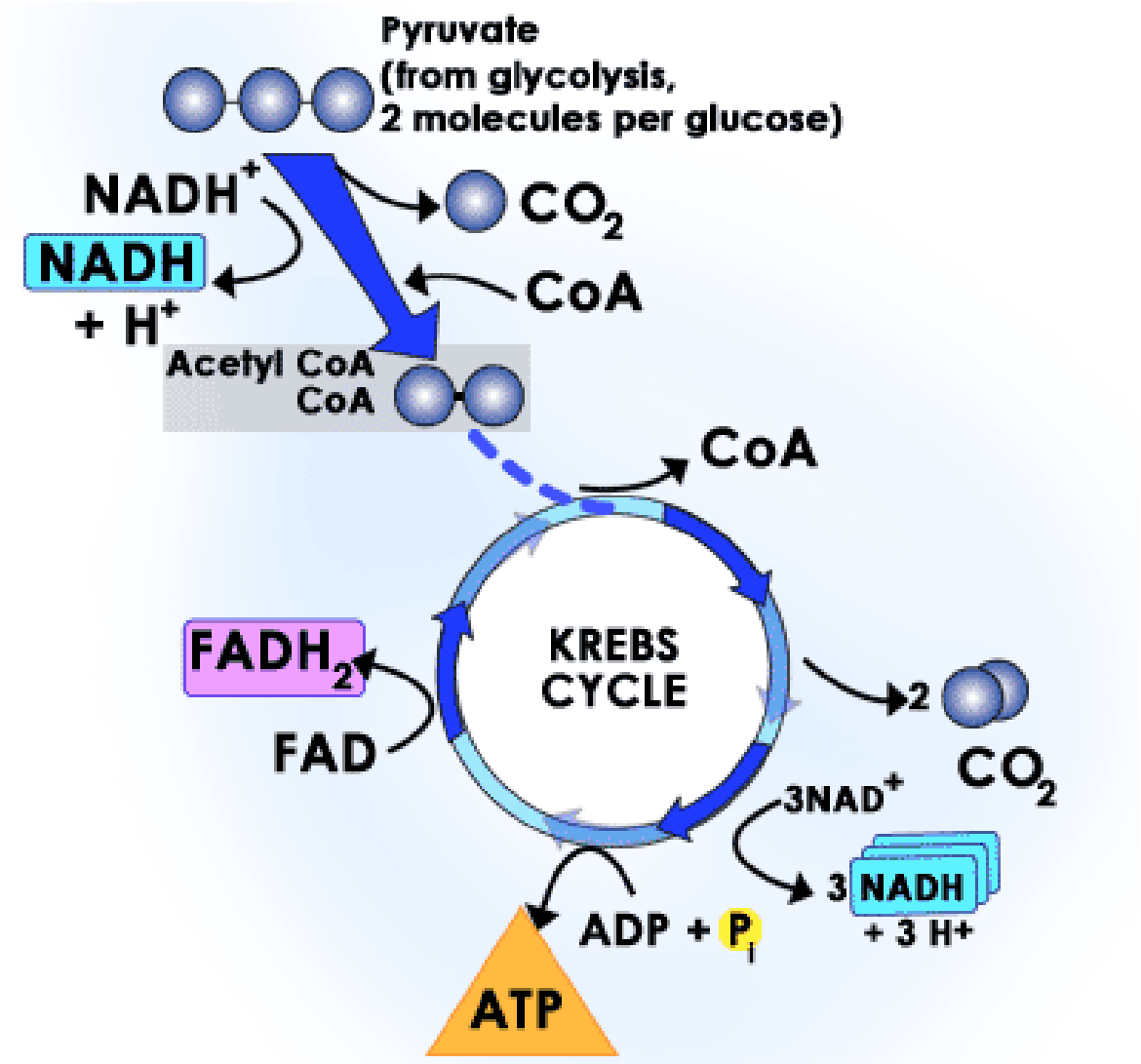
50% Dextrose

- ***Reasoning behind empiric administration of dextrose has been that irreversible brain damage may result from delays in treating hypoglycemia.***
- ***Also based on assumption that dextrose is harmless to persons with normal or elevated blood glucose levels.***

50% Dextrose

- ***Research has shown that people who receive glucose solutions before or during episodes of brain ischemia tend to have more significant neurological damage when compared to patients who only received saline solution.***


glucose
ATP
1
glucose 6-phosphate
2
fructose 6-phosphate
3
fructose 1,6-diphosphate
4
2x
glyceraldehyde 3-phosphate
2
P
2
NADH
5
2x
1,3-diphosphoglycerate
2
ATP
6
2x
3-phosphoglycerate
7
2x
2-phosphoglycerate
8
2x
phosphoenolpyruvate
2
ATP
9
2x
pyruvate


Pyruvate
(from glycolysis,
2 molecules per glucose)
NADH+
NADH
+ H+
CO2
CoA
Acetyl CoA
CoA
CoA
KREBS
CYCLE
FADH2
FAD
2
CO2
3NAD+
3 NADH
+ 3 H+
ADP + Pi
ATP

50% Dextrose

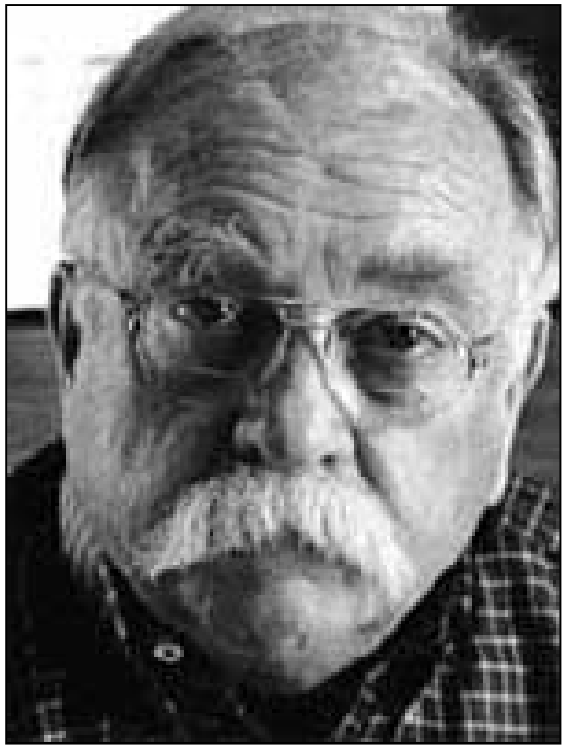
- ***Administering a large glucose load during periods of ischemia floods the brain with glucose molecules that are converted to puruvic acid, then lactic acid.***
- ***Localized acidosis can cause neurological damage to delicate brain tissues.***

50% Dextrose

- ***The technology to rapidly assess blood glucose levels should be available in every EMS unit in the country.***

50% Dextrose

- ***If Wilford Brimley can check his blood sugar (and do it often) then we can too!***



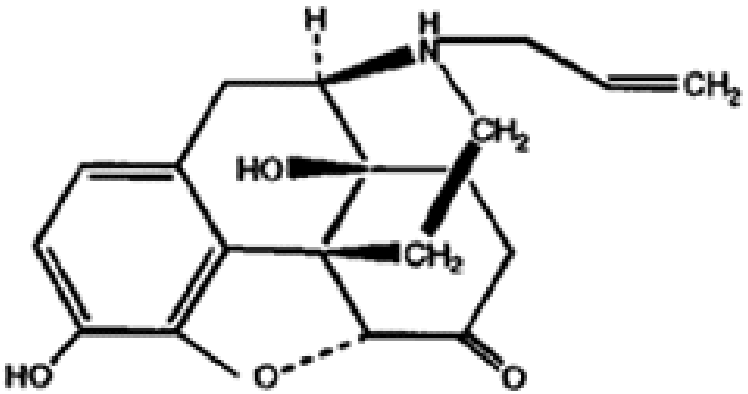
50% Dextrose

- ***It is important to point out that non-diabetic bonafide hypoglycemia can develop in babies and young children due to stress and infection.***
- ***Because of this, babies and young children should be approached with a higher index of suspicion.***

50% Dextrose

- ***When in doubt—give 50% dextrose (but try not to be in doubt!)***

Naloxone (Narcan)



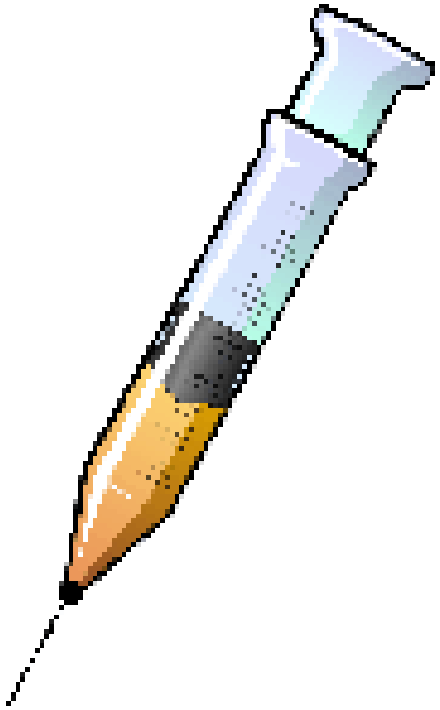
Naloxone (I.S.)

- ***Used for reversal of respiratory depression associated with narcotic overdose.***
- ***Used for reversal of respiratory depression associated with synthetic opioid compounds (Darvon, Nubain, Stadol).***

Naloxone (Narcan)

- ***Ineffective in reversing coma due to other causes.***

Naloxone (Narcan)



- ***Narcotic overdose should be fairly easy to recognize in the field setting:***
  - ***Constricted pupils***
  - ***Respiratory depression***
  - ***Cardiovascular depression***
  - ***Location of call (“shooting gallery”)***
  - ***Paraphenalia***
  - ***Needle tracks***

Naloxone (Narcan)

- ***Goal of prehospital naloxone therapy is to simply reverse respiratory depression.***
- ***Overzealous administration will induce full-blown narcotic withdrawal that will be very unpleasant for all involved.***
- ***Thus, should only be administered in small, titrated doses.***

Thiamine

- ***Thiamine became commonplace in EMS following a case report published in 1994.***
- ***Chronic alcohol abuser's confusion, difficulty ambulating, and visual disturbances spontaneously resolved following a single dose.***

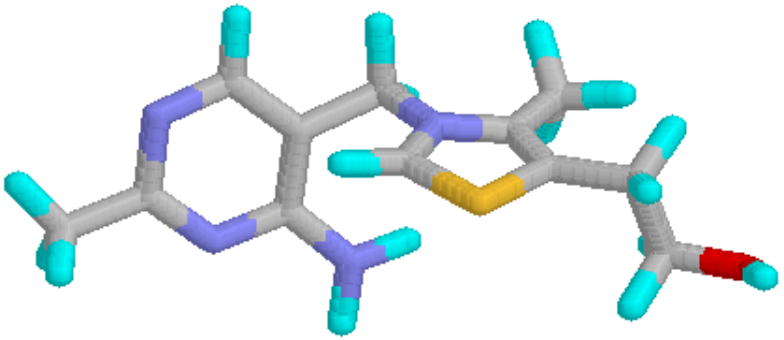
Thiamine

- ***How many have seen any change in patient condition following prehospital thiamine administration?***

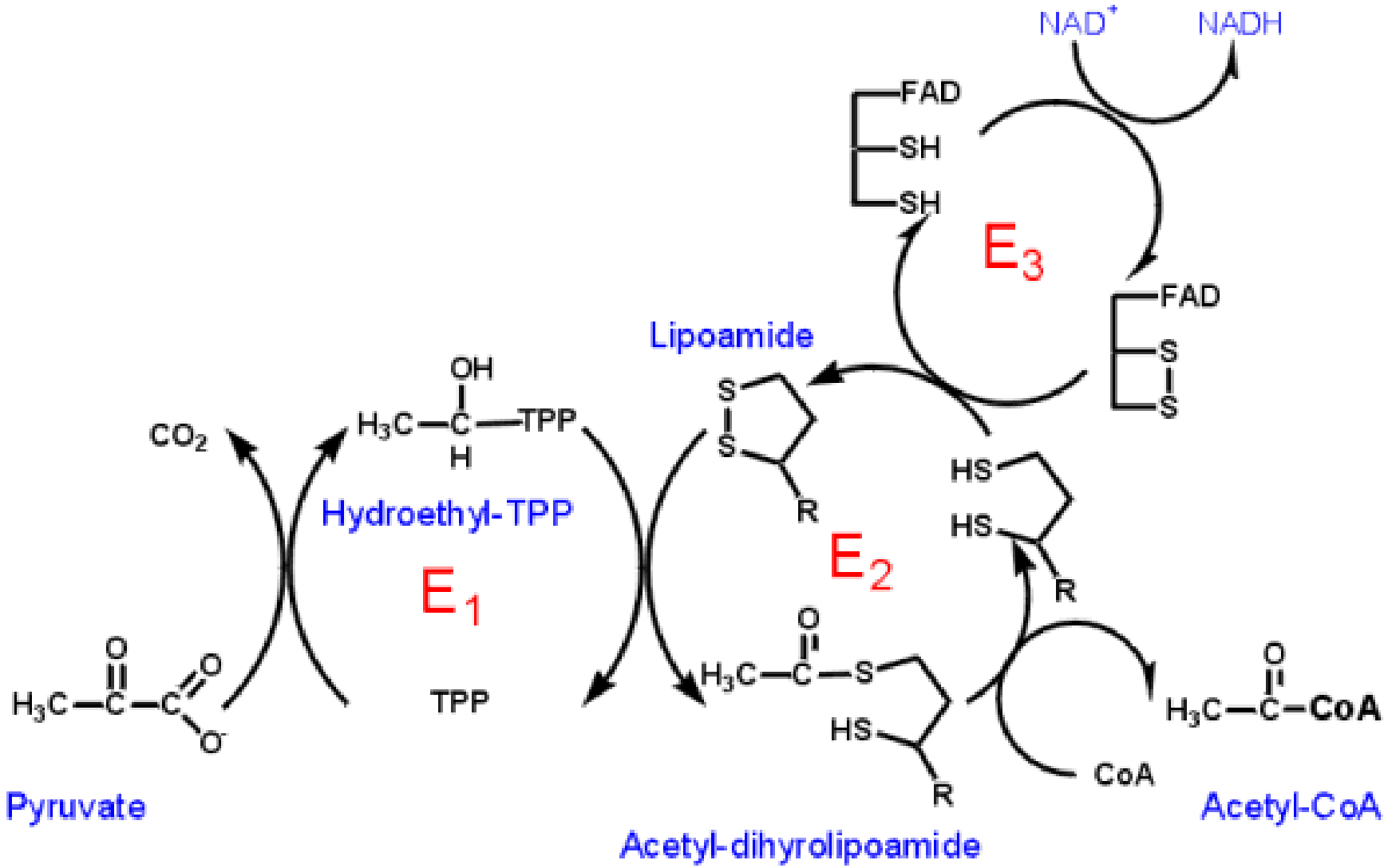
Thiamine

- ***A vitamin is a substance that the body needs for normal function, but cannot manufacture.***
- ***Must be obtained from the diet***
- ***Vitamin deficiencies cause well described problems such as scurvy & pernicious anemia.***

Thiamine



- ***Thiamine is essential for normal cellular metabolism and the proper utilization of glucose.***
- ***Thiamine is a co-factor that converts pyruvate into a form that can enter the Kreb's cycle.***



NAD+
NADH
FAD
SH
SH
E3
FAD
S
S
Lipoamide
OH
H3C—C—TPP
H
CO2
S
S
R
HS
HS
R
Hydroethyl-TPP
E1
E2
O
H3C—C—S
HS
R
O
H3C—C—CoA
CoA
O
H3C—C—C
O
O-
TPP
Pyruvate
Acetyl-dihyrolipoamide
Acetyl-CoA

Thiamine

- ***Alcoholics tend to get most of their calories and nutrition through alcohol products.***
- ***In this country, alcohol products are not fortified.***
- ***Alcohol can impair absorption of thiamine and other vitamins.***

Thiamine

- ***Thiamine deficiency:***
  - **Wernicke's Encephalopathy *(acute thiamine deficiency):***
    - **Triad of opthalmoplegia, ataxia, and altered mental status**
    - **Triad only seen in a small number of cases**
    - **Due to death of selected nerve cells in various parts of the brain**

Thiamine

- ***Thiamine deficiency:***
  - **Korsakoff's Psychosis *(chronic thiamine deficiency)***
    - **Amnesia**
    - **Confabulation**
    - **Irreversible**

Thiamine

- ***Wernicke's encephalopathy can be reversed with thiamine, but Korsakoff's psychosis, once developed, is often irreversible.***

Thiamine

- ***So what's the problem with empiric thiamine administration?***
  1. ***Incidence of WE is relatively rare (< 0.2%)***
  2. ***Although most WE patients have altered mental status, few present with coma.***
  3. ***Cases of severe anaphylactic reactions to intravenous thiamine have been reported.***
  4. ***To fully reverse symptoms of WE, thiamine must be administered over a period of 3 days.***

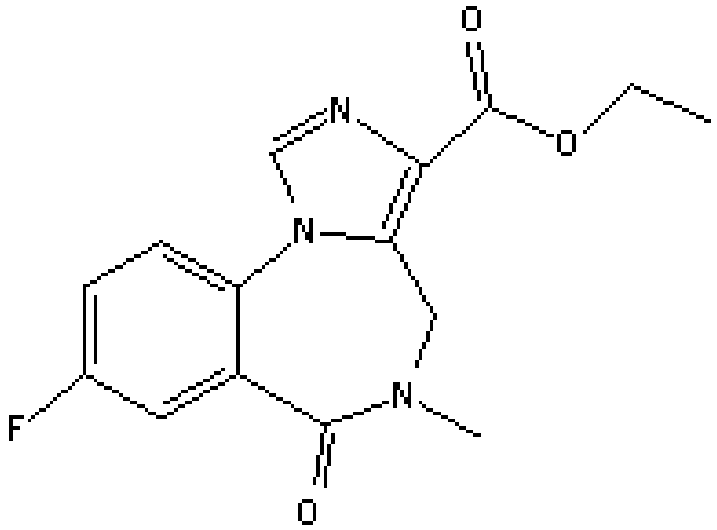
Thiamine

- ***Thiamine has a very limited role in EMS and is probably a waste of resources.***
- ***Money would be better spent to fortify cheap wines and liquors.***

Thiamine

- ***Many countries have fortified flour with thiamine.***
- ***In Sydney, NSW, Australia, the incidence of KP and WE were reduced by 40% following the fortification of flour with thiamine.***

Flumazenil



- ***Less common ingredient in the "coma cocktail."***
- ***Benzodiazepine antagonist.***

Flumazenil

- ***Overdoses of benzodiazepines cause:***
  - ***Altered mental status***
  - ***Slurred speech***
  - ***Dysrhythmias***
  - ***Coma***
- ***Benzodiazepine drugs:***
  - ***Diazepam (Valium)***
  - ***Lorazepam (Ativan)***
  - ***Alprazolam (Xanax)***

Flumazenil

- ***Benzodiazepines are among the most prescribed drugs in modern medical practice.***
- ***Uses:***
  - ***Anxiety disorders***
  - ***Sleep disorders***
  - ***Muscle relaxants***

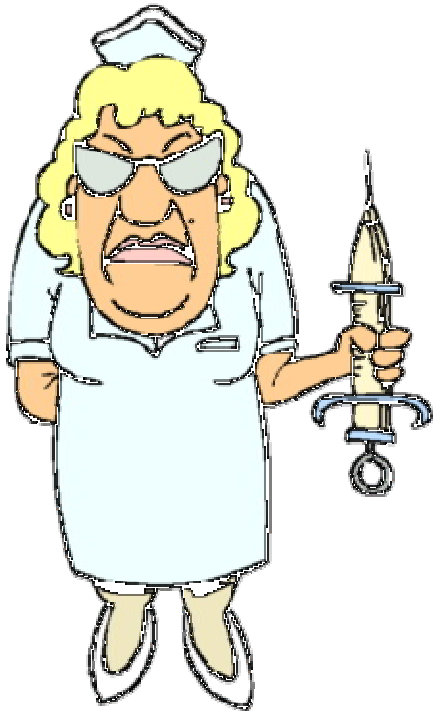
Flumazenil

- ***Many people are benzodiazepine-dependent.***
- ***Sudden reversal with flumazenil can cause a dangerous benzodiazepine withdrawal:***
  - ***Tremors***
  - ***High levels of anxiety***
  - ***Muscle jerks***
  - ***Seizures***

Flumazenil

- ***Because of this, flumazenil should NEVER be part of a so-called "Coma Cocktail" or given empirically!***

"Coma Cocktail"



- ***EMS has evolved far enough where silliness, such as "coma cocktails" should be abolished from prehospital practice!***

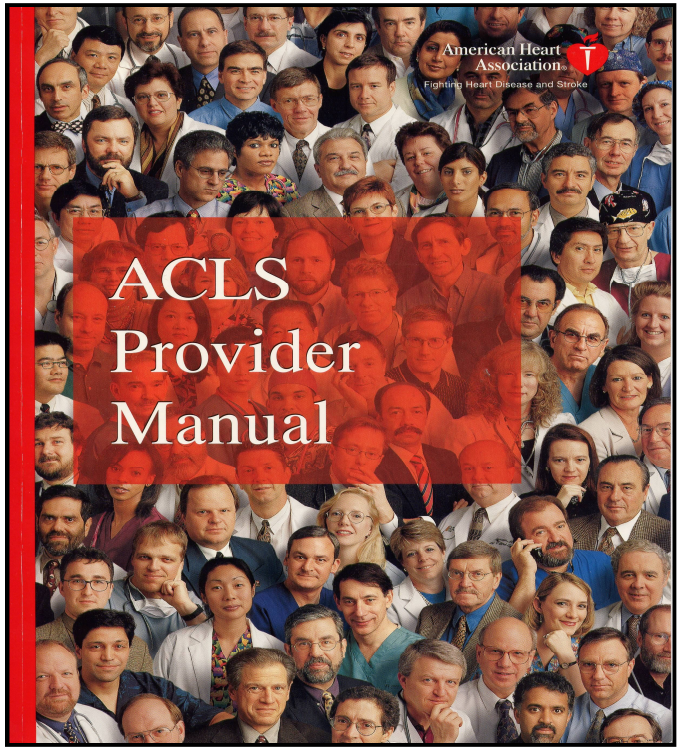
"Coma Cocktail"

- ***Summary:***
  - ***"Coma Cocktails" are a BAD idea.***
  - ***EMS personnel should be able to narrow down potential causes of coma.***
  - ***Hypoglycemia (or suspected hypoglycemia) should be aggressively treated.***
  - ***Naloxone should ONLY be used for possible narcotic overdoses.***
  - ***Thiamine should ONLY be used in patients suspected of chronic alcohol abuse and exhibit signs of WE.***
  - ***Flumazenil has NO ROLE in the prehospital treatment of coma.***

tPA for CVA

- ***Is thrombolytic therapy is the standard of care for stroke patients today?***

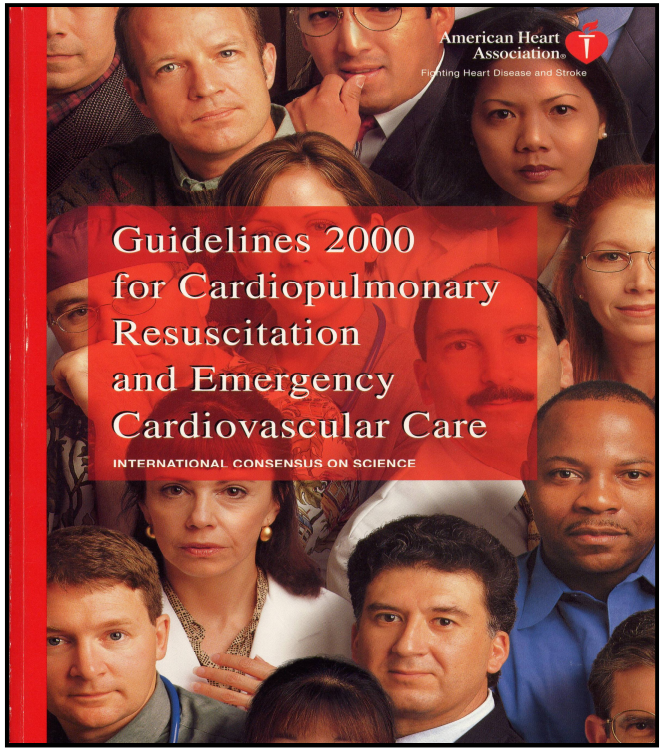
tPA for CVA



- ***The AHA stated, "Research has continued to accumulate in support of the effect of thrombolytic therapy when given to carefully selected patients within 3 hours of the onset of acute ischemic stroke."***

tPA for CVA

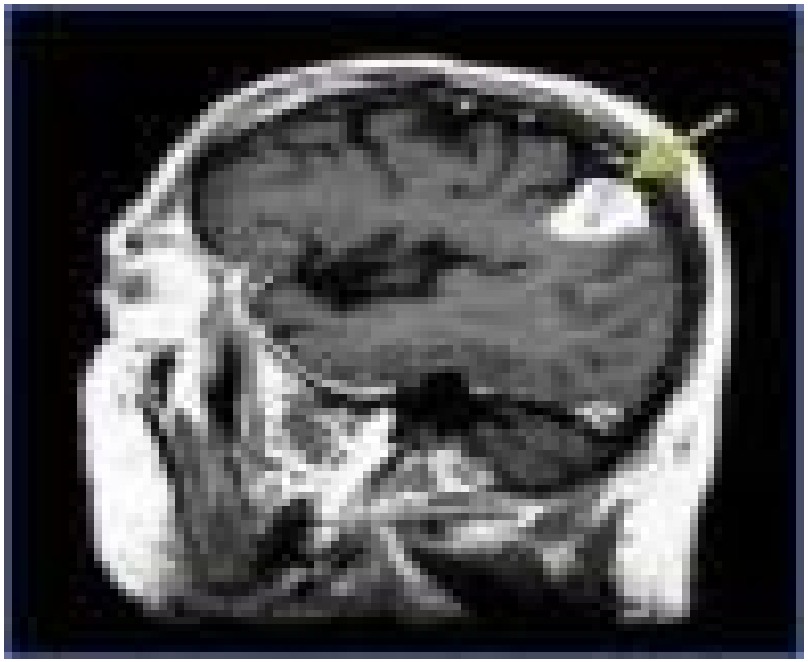
- ***Is there a conflict of interest at the AHA?***
  - ***Genentech, the manufacturer of tPA, donated $11 million to the AHA in the decade prior to AHA recommending tPA for stroke***
  - ***Most of the association's stroke experts have ties to the manufacturer of tPA.***



tPA for CVA

- ***Since the NINDS trial, there has not been one confirmatory study to demonstrate the effectiveness of thrombolytic therapy for acute ischemic stroke.***

  - The N.I.N.D.S rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke.* N Eng J Med. *1995;333:1581-1587



tPA for CVA

- ***There have been a total of six multi-center trials of thrombolytics since the 1980s in the United States, Europe, Australia, and China.***
- ***The NINDS trial was the first and only one to demonstrate a positive benefit.***

tPA for CVA

- ***The only study not sponsored by a drug company had different results:***
  - ***A study involving every single stroke patient treated at 29 Cleveland-area non-VA hospitals over a 1 year period.***
  - ***Only 1.8% (70 of 3948 patients) received tPA. Of these, only half (<1%) actually met the NINDS criteria.***

tPA for CVA

- ***The only study not sponsored by a drug company had different results:***
  - ***The results were strikingly different from the NINDS trial, and extremely negative.***
  - ***The rate of symptomatic intracerebral hemorrhage was 15.7% (compared to 7.2% in the control group). Six of these were fatal.***

- Katzen et al. Use of tissue-type plasminogen activator for acute ischemic stroke: The Cleveland area experience.* JAMA. *2000; 283(9):1151-1158

tPA for CVA

- ***The Canadian Association of Emergency Physicians guidelines state, "thrombolytic therapy should be restricted to use in the context of formal research protocols, or in a closely monitored program"***

tPA for CVA

- ***"Since the NINDS trial there has not been a second randomized, double-blinded, placebo-controlled study to validate its findings. There is insufficient evidence at this time to endorse the use of intravenous tPA in clinical practice…"***

American College of Emergency Physicians®

tPA for CVA

- ***"It is the position of the American Academy of Emergency Medicine that objective evidence regarding the efficacy, safety, and applicability of tPA for acute ischemic stroke is insufficient to warrant its classification as a standard of care."***

tPA for CVA

- ***Following public scrutiny, the American Heart Association recently withdrew statements that tPA for stroke "saves lives."***

tPA for CVA

- ***The role of tPA in acute ischemic stroke is very limited.***
- ***Thrombolytic therapy for acute ischemic stroke is probably best limited to tertiary facilities with a neuroradiologist reading the films and a neurologist administering the therapy.***
- ***tPA for acute ischemic stroke is not the standard of care.***